Complete Summary

GUIDELINE TITLE

Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Aug. 21 p. (Technology appraisal guidance; no. 127).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 27, 2008, Tysabri (natalizumab): U.S. Food and Drug Administration (FDA) and Biogen Idec, Elan notified healthcare professionals of reports of clinically significant liver injury as early as six days after the first dose of Tysabri. These injuries may lead to death or the need for a liver transplant in some patients. Tysabri should be discontinued in patients with jaundice or other evidence of significant liver injury. Physicians should inform patients that Tysabri may cause liver injury.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Highly active relapsing–remitting multiple sclerosis (RES)

Note: RES is defined by two or more disabling relapses in 1 year, and one or more gadolinium-enhancing lesions on brain magnetic resonance imaging (MRI) or a significant increase in T2 lesion load compared with a previous MRI.

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of natalizumab in the treatment of highly active relapsing–remitting multiple sclerosis

TARGET POPULATION

Patients with rapidly evolving severe relapsing–remitting (RES) multiple sclerosis

INTERVENTIONS AND PRACTICES CONSIDERED

Natalizumab for patients with rapidly evolving severe (RES) relapsing–remitting multiple sclerosis

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Disability progression rate
    - Annualized relapse rate

    - Health-related quality of life
    - Adverse effects
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Peninsula Technology Assessment Group, Peninsula Medical School and Wessex Institute for Health Research and Development, University of Southampton (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description of Search Strategies and Comment on Whether the Search Strategies Were Appropriate

Clinical Effectiveness Searches for Comparators

Detailed search strategies and results are provided, including the biomedical databases searched – Medline, Medline in Process, Embase and Cochrane Central, the time frame of the searches and host interface (Ovid) used. Suitable search terms were used with controlled language and text words. The searches are limited by randomised controlled trial (RCT) study and by year from 2001. The search strategies appear sound and reproducible.

The Evidence Review Group (ERG) assessed whether or not there was additional trial data using the searches shown in Appendix 2 of the ERG report (see the "Availability of Companion Documents" field). Fifty-three references were identified for glatiramer acetate (GA) and 305 for beta-interferon (IFN-beta) through these update searches. After screening all abstracts and two full text papers, the ERG did not identify any additional trials of IFN-beta or GA that should have been included.

Statement of the Inclusion and Exclusion Criteria and Comment on Whether They Were Appropriate

No explicit inclusion criteria were applied to the studies identified. Biogen have included in their submission RCT data about natalizumab in adults with relapsing-remitting multiple sclerosis (RRMS) and secondary progressive multiple sclerosis (SPMS), as mono- or combination therapy, with follow up of at least 12 weeks,

where natalizumab is taken as a monthly-dose course. Trials that describe single dose use of natalizumab during relapse are not included.

The four trials included in the submission, and their outcome measures, are shown in Table 1 of the ERG Report (see the "Availability of Companion Documents" field).

Comparators

Cochrane reviews were used as the basis for evidence about the effectiveness of the two active comparators, IFN-beta and GA. Searches for these reviews were updated by the manufacturer, using a more limited population than the original in order to restrict trials to adult RRMS populations with relevant outcomes. No additional trials were identified for inclusion in the IFN-beta review.

Ongoing Studies

Biogen reports on three ongoing studies relevant to the submission. One is an open label extension of the AFFIRM and SENTINEL trials. Two are prospective, observational cohort studies. Safety is the primary interest of these studies.

Refer to Sections 4.1.1 to 4.1.4 of the ERG Report (see the "Availability of Companion Documents" field) for more information.

Cost-Effectiveness

A systematic review of economic evaluations of natalizumab was undertaken by Biogen. This searched an acceptable core of databases (Medline, Medline in process, Embase and National Health Service Economic Evaluation Database [NHS EED]). Details of the searches, including their time frame and language limits are described, and allow the searches to be reproduced. The search did not identify any economic evaluations for natalizumab.

NUMBER OF SOURCE DOCUMENTS

- The manufacturer identified 4 studies.
- The Evidence Report Group (ERG) identified an additional combination therapy trial.
- Biogen reports on three ongoing studies relevant to the submission.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Peninsula Technology Assessment Group, Peninsula Medical School and Wessex Institute for Health Research and Development, University of Southampton (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description and Critique of the Manufacturer's Approach to Validity Assessment

The manufacturer uses items based on the CONSORT statement to critically appraise the randomised controlled trials (RCTs) of both natalizumab and comparators. They also provide a Jadad score. The submission concludes that the trials of natalizumab are as good or better than those for the comparators although, as they themselves note, as they have access to trial information on their own databases, this is perhaps not surprising – all assessment of comparators were based on the published trial reports only.

The conclusion that the natalizumab trials are well conducted is reasonable (refer to the assessment of quality in Appendix 3 of the ERG report) (see the "Availability of Companion Documents" field). Methods of randomisation and blinding were adequate, and although there was some drop out, this was small and similar in both arms. However, little consideration is given to relevant external validity. The assessment concludes that epidemiology of multiple sclerosis (MS) in the multicentre trial is likely to be similar to that in the UK but do not note that the studied population does not match the licensed populations.

Description and Critique of the Manufacturer's Statistical Approach

The statistical analysis of the AFFIRM trial was well reported.

The AFFIRM trial was adequately powered. The sample size was based on 90% power to detect an assumed annualised relapse rate of 0.6 with natalizumab and 0.9 with placebo with 15% drop out and required 900 people at 5% significance. Progression rates at the end of two years were assumed to be 35% with placebo and 23% with natalizumab. These effect sizes were met in the trial.

Appropriate statistical methods were used to compare the two groups. The U.S. Food and Drug Administration (FDA) statistical review did raise the issue that since randomisation was stratified by site, site should have been incorporated as a covariate in the primary analysis. However, such adjustment is not statistically

mandatory and as the FDA statistical reviewers concede, sparse data in some sites may have made such adjustment for centres problematic.

The rapidly evolving severe (RES) subgroup is based on a smaller subgroup of the AFFIRM trials (n=209). As the impact of natalizumab is greater than predicted, significant results are seen in this subgroup. Details of withdrawals are not given.

Data Syntheses

The submission does not statistically pool information about natalizumab treatment effect and this is appropriate given the different treatment and comparator regimes in the AFFIRM and SENTINEL trials, and the short term follow up in the MS201 and 231.

The submission does pool information from AFFIRM, MS201 and MS231 on safety. As the length of follow-up in these three trials is different (2 years, 12 weeks and 24 weeks), it may have been more appropriate to use rate ratios, rather than the risk ratios used in the submission. Given the shorter follow up period in MS231 and MS201, it is possible that these trials may bias the results in favour of natalizumab, as there may be less adverse effects with less exposure to the drug.

Refer to Section 4 of the ERG Report (see the "Availability of Companion Documents" field) for more information.

Cost-Effectiveness

Overview/Summary of Manufacturer's Economic Assessment

The manufacturer submission reports cost effectiveness analyses (CEA), presenting cost per quality-adjusted life year (QALY) estimates for natalizumab compared to:

- Best supportive care (BSC) (BSC reflects the placebo arm of RCTs)
- Beta-interferon (IFN-beta)
- Glatiramer acetate (GA)

Cost per QALY estimates are presented for the RES and sub-optimal therapy (SOT) subgroups of patients with relapsing-remitting multiple sclerosis (RRMS).

The CEA uses a decision-analytic model (Markov-process cohort model) to estimate the incremental costs and benefits associated with natalizumab treatment, versus stated comparators. The main components of this model are summarised in the ERG Report (see the "Availability of Companion Documents" field).

Sensitivity Analysis

Extensive one-way sensitivity analysis is reported, plus multi-way sensitivity analysis and probabilistic sensitivity analysis (PSA). (Table 10 in the ERG Report [see the "Availability of Companion Documents" field])

Model Validation

The submission reports consideration of model validation, including tests for internal consistency, and consideration of the model in the context of model inputs (transit probabilities) and other analyses of disease modifying therapies (DMTs) for MS.

Critical Appraisal of Manufacturer's Economic Evaluation

Internal Consistency

The ERG has undertaken extensive checking of the Excel programming and mathematical logic of the model, and find the model to be well set out and accurate (with the exception of the items listed in the ERG Report [see the "Availability of Companion Documents" field]). All equations in the model have been checked for internal consistency/accuracy. The model is fully executable and the ERG has been able to replicate CEA results presented in the submission, the sensitivity analysis presented (in almost all scenarios), and the probabilistic sensitivity analysis presented.

External Consistency

The manufacturer submission reports that the external consistency of the model has been considered. The issue of validity is considered in the context of (1) external independent review, (2) predictions of the model compared to data inputs, and (3) consideration of model outputs against other studies of a similar nature.

The submission states that the methods used were valid. The submission compares AFFIRM data to the multi-state-model (MSM) used to derive transit probabilities, presenting evidence that the predictive power of the transit probabilities derived from the MSM model is high.

The ERG has concerns over the different rate of disability progression predicted in the manufacturer model and that presented in the AFFIRM trial against the primary endpoint of AFFIRM. They have undertaken additional analysis to compare the prediction of the model against the endpoint of the AFFIRM trial.

The ERG's analysis of the manufacturer's model shows a much higher cumulative probability of sustained disability progression (at 2-years) for the SOT subgroup than in the AFFIRM trial. Results show a cumulative probability of progression of 33% in the natalizumab treated group versus 53% for BSC (absolute risk reduction of 20%). A similar conclusion applies for the RES subgroup.

One-Way Sensitivity Analyses

The manufacturer submission and subsequent addendum present extensive sensitivity analyses on the key parameters in the model.

The ERG has checked all of these univariate-sensitivity analyses, and agrees with all except two. In the two cases shown in Table 16 of the ERG Report they find different cost per QALY data.

Refer to Section 5 of the ERG Report (see the "Availability of Companion Documents" field) for more information.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The manufacturer presented a multistate Markov model based on the economic model developed by the School of Health and Related Research (ScHARR) at Sheffield University that was used in 'Beta interferon and glatiramer acetate for the treatment of multiple sclerosis' (National Institute for Health and Clinical Excellence [NICE] technology appraisal 32). Data on costs and utilities (based on EQ-5D scores) associated with expanded disability status scale (EDSS) states were derived from a cross-sectional study (the UK multiple sclerosis [MS] survey) commissioned by the manufacturer.

The results of the manufacturer's analysis showed that the incremental cost-effectiveness ratios (ICERs) for the rapidly evolving severe relapsing-remitting multiple sclerosis (RES) group compared with best supportive care, beta interferon and glatiramer acetate were 44,600 pounds sterling, 32,000 pounds sterling and 34,600 pounds sterling per quality-adjusted life year (QALY) gained respectively. For the suboptimal therapy group the ICERs were 56,100 pounds sterling, 43,400 pounds sterling and 44,300 pounds sterling per QALY gained respectively.

Sensitivity analysis demonstrated that the variables that had the greatest effect on the ICERs were the time horizon over which costs and outcomes are evaluated and changing the source of the disability progression data from AFFIRM to the London Ontario dataset. Extending the time horizon to 30 years, for example, reduced the ICERs for natalizumab versus beta interferon to 24,600 pounds sterling and 34,200 pounds sterling per QALY gained in the RES and suboptimal therapy groups respectively. In contrast, changing the source of the disability progression data from AFFIRM to the London Ontario dataset increased the ICERs to 42,300 pounds sterling and 55,300 pounds sterling per QALY gained for natalizumab versus beta interferon in the RES and suboptimal therapy groups respectively.

Although the Committee had reservations about the data on the clinical effectiveness of natalizumab in the suboptimal therapy group (as indicated in

section 4.2 of the original guideline document), it reviewed the manufacturer's cost-effectiveness analysis for this group and the Evidence Review Group's (ERG's) comments. The Committee noted that the base case ICERs estimated by the manufacturer for the suboptimal therapy group were 43,400 pounds sterling per QALY gained or higher. It therefore concluded that natalizumab would not be a cost-effective use of National Health Service (NHS) resources in this group of people.

The Committee noted that the base case ICERs estimated for the rapidly evolving severe (RES) group by the manufacturer ranged from 32,000 pounds sterling per QALY gained (natalizumab compared with beta interferon) to 44,600 pounds sterling per QALY gained (natalizumab compared with best supportive care).

The Committee noted the views of the ERG that the results of the manufacturer's economic model were associated with considerable uncertainty and that alternative assumptions would substantially increase or decrease the ICERs. The Committee took into account the high degree of clinical need among people in the RES group and the innovative nature of the technology. The Committee therefore concluded that the use of natalizumab for people with RES would be a cost-effective use of NHS resources and that it should be recommended for use within the NHS for the treatment of people with RES.

Refer to Sections 3 and 4 in the original guideline document for more information.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Natalizumab is recommended as an option for the treatment only of rapidly evolving severe relapsing–remitting multiple sclerosis (RES). RES is defined by two or more disabling relapses in 1 year, and one or more gadolinium-enhancing

lesions on brain magnetic resonance imaging (MRI) or a significant increase in T2 lesion load compared with a previous MRI.

People currently receiving natalizumab, but for whom treatment would not have been recommended according to the above section of this guidance, should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

CLINICAL ALGORITHM(S)

An algorithm is provided in the Evidence Review Group Report for: Possible disease development and place of treatment with natalizumab (see "Availability of Companion Documents" field).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

One randomized controlled trial, the AFFIRM trial, comparing natalizumab with placebo in people with relapsing remitting multiple sclerosis, is the basis for the recommendation on clinical effectiveness.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of natalizumab for the treatment of highly active relapsing–remitting multiple sclerosis

POTENTIAL HARMS

The use of natalizumab may be associated with infections, urticaria, headache, dizziness, vomiting, nausea, arthralgia, infusion reactions and hypersensitivity reactions. Natalizumab has also been associated with an increased risk of progressive multifocal leukoencephalopathy (PML).

For full details of side effects and contraindications, see the summary of product characteristics available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances

of the individual patient, in consultation with the patient and/or guardian or carer.

- Limitations and areas of uncertainty of the submitted evidence:
    - There is no direct evidence about the use of natalizumab among the sub-optimal therapy (SOT) group.
    - Evidence for the rapidly evolving severe (RES) group is based on a subgroup analysis of one randomised controlled study (RCT).
    - There are no head to head comparisons of natalizumab with other active therapies.
    - The Evidence Review Group (ERG) is unsure about the appropriateness of some of the data used to populate the model for the patient group under consideration.
    - Although frequently used, the Expanded Disability Status Scale, on which the model is based, has some well known limitations.
    - The effect of natalizumab compared with active treatments is uncertain – indirect comparisons among people with highly active multiple sclerosis (MS) show wide confidence intervals, that include no benefit, around the key outcome of disease progression.
    - Underlying disease progression in the model is based on data from the AFFIRM trial and should be treated with caution.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for Better Health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on NICE website (www.nice.org.uk).
    - Costing template incorporating a costing report to estimate the savings and costs associated with implementation.
    - Audit criteria to monitor local practice.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Aug. 21 p. (Technology appraisal guidance; no. 127).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Aug

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor Keith Abrams, Professor of Medical Statistics, University of Leicester; Dr Jeff Aronson, Reader in Clinical Pharmacology, Radcliffe Infirmary; Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Professor David Barnett (Chair), Professor of Clinical Pharmacology, University of Leicester; Dr Peter Barry, Consultant in Paediatric Intensive Care, Leicester Royal Infirmary; Professor Stirling Bryan, Director of the Health Economics Facility, University of Birmingham; Professor John Cairns, Public Health and Policy, London School of Hygiene and Tropical Medicine; Dr Mark Charkravarty, Head of Government Affairs and NHS Policy, Procter and Gamble Pharmaceuticals (UK); Professor Jack Dowie, Health Economist, London School of Hygiene and Tropical Medicine; Lynn Field, Nurse Director, Pan Birmingham Cancer Network; Professor Christopher Fowler, Professor of Surgical Education, University of London; Dr Fergus Gleeson, Consultant Radiologist, Churchill Hospital, Oxford; Ms Sally Gooch, Former Director of Nursing and Workforce Development, Mid Essex Hospitals Services NHS Trust; Mrs Barbara Greggains, Lay member; Mr Sanjay Gupta, Former Stroke Services Manager, Basildon and Thurrock Universities Hospitals NHS Trust; Dr Mike Laker, Medical Director, Newcastle Hospitals NHS Trust; Mr Terence Lewis, Mental Health Consultant, National Institute for Mental Health in England; Professor Gary McVeigh, Professor of Cardiovascular Medicine, Queens University, Belfast; Dr Ruairidh Milne, Senior Lecturer in Health Technology Assessment, National Coordinating Centre for Health Technology; Dr Neil Milner, General Medical Practitioner, Sheffield; Dr Rubin Minhas, General Practitioner, CHD Clinical Lead, Medway PCT; Dr John Pounsford, Consultant Physician, North Bristol NHS Trust; Dr Rosalind Ramsay, Consultant Psychiatrist, Adult Mental Health Services, Maudsley Hospital, London; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Dr Lindsay Smith, General Practitioner, East Somerset Research Consortium; Mr Cliff Snelling, Lay member; Dr Ken Stein, Senior Lecturer, Peninsula Technology Assessment Group (PenTAG), University of Exeter; Professor Andrew Stevens, Professor of Public Health, University of Birmingham

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Natalizumab for the treatment of adults with highly active relapsing—remitting multiple sclerosis. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Aug. 1 p. (Technology appraisal 127). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Natalizumab for the treatment of adults with highly active relapsing—remitting multiple sclerosis. Costing template and report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Aug. 19 p. (Technology appraisal 127). Available in Portable Document Format (PDF) from the NICE Web site.
- Natalizumab for the treatment of adults with highly active relapsing—remitting multiple sclerosis. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Aug 20. 9 p. (Technology appraisal 127). Available in Portable Document Format (PDF) from the NICE Web site.
- The effectiveness and cost-effectiveness of natalizumab for multiple sclerosis: an evidence review of the submission from biogen. Evidence Review Group report. School of Health and Related Research (ScHARR). University of Sheffield, Sheffield, UK; 2007 Feb 6. 133 p. (Technology appraisal 127). Available in Portable Document Format (PDF) from the NICE Web site.
- Guide to the single technology appraisal process. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Sept 19. 44 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: TA127, 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Natalizumab for the treatment of adults with highly active relapsing—remitting multiple sclerosis. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Aug. 4 p. (Technology appraisal 127).

Available in Portable Document Format (PDF) from the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on October 16, 2007. This summary was updated by ECRI Institute on March 6, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Tysabri (natalizumab).

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Technology Appraisal guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE technology appraisal guidance is prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 9/29/2008